

(19) World Intellectual Property Organization  
International Bureau



PCT



(43) International Publication Date  
23 February 2006 (23.02.2006)

(10) International Publication Number  
**WO 2006/020919 A3**

(51) International Patent Classification:  
C12N 5/00 (2006.01) C12N 5/06 (2006.01)

(21) International Application Number:  
PCT/US2005/028829

(22) International Filing Date: 15 August 2005 (15.08.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/601,664 13 August 2004 (13.08.2004) US

(71) Applicants (for all designated States except US):  
**UNIVERSITY OF GEORGIA RESEARCH FOUNDATION, INC.** [US/US]; 627A Boyd Graduate Studies Research Center, Athens, Georgia 30602-7411 (US).  
**CYTHERA, INC.** [US/US]; 3550 General Atomics Court, San Diego, California 92121 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **DALTON, Stephen** [AU/US]; 1030 Coday Bluff, Athens, Georgia 30606 (US). **SHEPPARD, Allan** [GB/US]; 611 Hidden Lakes Trail, Jefferson, Georgia 30459 (US). **JONES, Karen** [AU/US]; 237 Springdale Street, Athens, Georgia 30606 (US). **BAETGE, E., Edward** [US/US]; 308 Sunset Drive,

Encinitas, California 92024 (US). **D'AMOUR, Kevin, A.** [US/US]; 2739 East Evans Road, San Diego, California 92106 (US). **AGULNICK, Alan, D.** [US/US]; 1259 Stratford Court, San Marcos, California 92069 (US).

(74) Agents: **WARREN, William, L.** et al.; Sutherland Asbill & Brennan LLP, 999 Peachtree Street, NE, Atlanta, Georgia 30309-3996 (US).

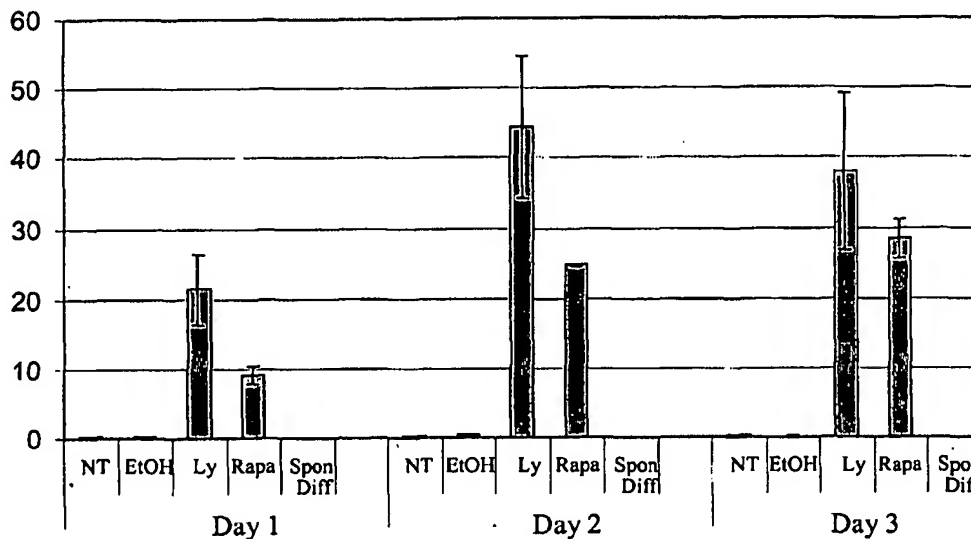
(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT,

[Continued on next page]

(54) Title: COMPOSITIONS AND METHODS FOR SELF-RENEWAL AND DIFFERENTIATION IN HUMAN EMBRYONIC STEM CELLS

SOX17/Norm



(57) Abstract: The present invention provides compositions and methods for the production of differentiated mammalian cells. More particularly, the present invention provides cellular differentiation methods employing culturing the cells on a feeder layer or under feeder-free conditions in cell culture and further contacting the cells with an inhibitor of the PI3-kinase pathway and a member of the TGF $\beta$  family for the generation of differentiated mammalian cells from pluripotent mammalian stem cells. Preferably, the differentiated cell is selected from the group consisting of a mesendodermal cell, a mesodermal cell, and an endodermal cell.



RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

(88) Date of publication of the International search report:

5 July 2007

**Published:**

- *with international search report*
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*